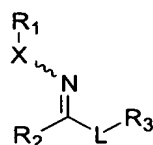


WHAT IS CLAIMED IS:

1. A compound of formula (I)



(I)

or a pharmaceutically acceptable salt or prodrug thereof, wherein

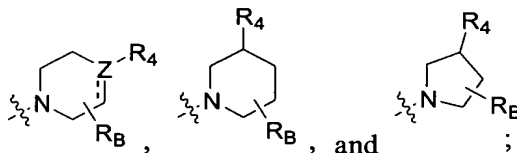
X is selected from the group consisting of O and NR<sub>A</sub>;

R<sub>A</sub> is selected from the group consisting of hydrogen and alkyl;

R<sub>1</sub> is selected from the group consisting of hydrogen, alkenyl, alkoxyalkyl, alkyl, alkynyl, arylalkyl, cyanoalkyl, cycloalkyl, haloalkyl, and hydroxyalkyl;

R<sub>2</sub> is selected from the group consisting of aryl, arylalkyl, heteroaryl, and heteroarylalkyl;

R<sub>3</sub> is selected from the group consisting of



R<sub>4</sub> is heteroaryl;

L is C<sub>1</sub>-C<sub>2</sub> alkylene substituted with 0 or 1 substituent selected from the group consisting of alkoxy, alkoxyamino, hydroxy, and hydroxyiminoaryl;

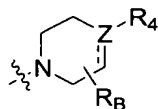
R<sub>B</sub> is selected from the group consisting of hydrogen and alkyl;

Z is selected from the group consisting of C, CH, and N; and

--- is absent or a single bond provided that when --- is a single bond then Z is

C.

2. The compound according to claim 1 wherein R<sub>3</sub> is



3. The compound according to claim 2 wherein

X is O;

R<sub>2</sub> is aryl;  
Z is N;  
--- is absent; and  
R<sub>4</sub> is heteroaryl.

5

4. The compound according to claim 2 wherein  
X is O;

R<sub>2</sub> is aryl wherein the aryl is selected from the group consisting of naphthyl  
and phenyl wherein the phenyl is substituted with 0, 1, or 2 substituents independently  
10 selected from the group consisting of alkyl, cyano, and halogen;

Z is N;  
--- is absent; and

R<sub>4</sub> is heteroaryl wherein the heteroaryl is selected from the group consisting of  
pyrazin-2-yl, 3-cyanopyridin-2-yl, 5-hydroxypyridin-2-yl, 3-methylpyridin-2-yl,  
15 pyridin-2-yl, 2-pyridinium N-oxide, pyrimidin-2-yl, and thiazol-2-yl.

5. The compound according to claim 4 selected from the group consisting of  
(1E)-1-(3-chlorophenyl)-3-(4-pyridin-2-yl-piperazin-1-yl)propan-1-one O-  
methyloxime;

20 (1Z)-1-(3-chlorophenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-  
methyloxime;

(1E)-1-(4-chlorophenyl)-3-(4-pyridin-2-yl-piperazin-1-yl)propan-1-one O-  
methyloxime;

25 (1Z)-1-(4-chlorophenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-  
methyloxime;

(1E)-1-(4-fluorophenyl)-2-(4-pyridin-2-ylpiperazin-1-yl)ethanone O-  
methyloxime;

(1Z)-1-(4-fluorophenyl)-2-(4-pyridin-2-ylpiperazin-1-yl)ethanone O-  
methyloxime;

30 (1E)-1-(4-chlorophenyl)-2-(4-pyridin-2-ylpiperazin-1-yl)ethanone O-  
methyloxime;

(1Z)-1-(4-chlorophenyl)-2-(4-pyridin-2-ylpiperazin-1-yl)ethanone O-  
methyloxime;

(1E)-1-(3,4-dimethylphenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-methyloxime;

(1Z)-1-(3,4-dimethylphenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-methyloxime;

5 (1E)-1-(3-chloro-4-fluorophenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-methyloxime;

(1Z)-1-(3-chloro-4-fluorophenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-methyloxime;

10 (1E)-1-(3-methylphenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-methyloxime;

(1Z)-1-(3-methylphenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-methyloxime;

(1E)-1-(4-fluorophenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-methyloxime;

15 (1Z)-1-(4-fluorophenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-methyloxime;

(1E)-1-(3,4-dichlorophenyl)-2-(4-pyridin-2-ylpiperazin-1-yl)ethanone O-methyloxime;

20 (1Z)-1-(3,4-dichlorophenyl)-2-(4-pyridin-2-ylpiperazin-1-yl)ethanone O-methyloxime;

(1E)-1-(2-methylphenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-ethyloxime;

(1Z)-1-(2-methylphenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-ethyloxime;

25 (1E)-1-(2-methylphenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-methyloxime;

(1Z)-1-(2-methylphenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-methyloxime;

30 3-[(1E)-N-methoxy-3-(4-pyridin-2-ylpiperazin-1-yl)propanimidoyl]benzonitrile

3-[(1Z)-N-methoxy-3-(4-pyridin-2-ylpiperazin-1-yl)propanimidoyl]benzonitrile

(1E)-1-(2,4-dichlorophenyl)-2-(4-pyridin-2-ylpiperazin-1-yl)ethanone O-methyloxime;

(1Z)-1-(2,4-dichlorophenyl)-2-(4-pyridin-2-ylpiperazin-1-yl)ethanone O-methyloxime;

(1E)-1-phenyl-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one oxime;

(1Z)-1-phenyl-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one oxime;

5 1,5-diphenyl-2-[(4-pyridin-2-ylpiperazin-1-yl)methyl]pentane-1,5-dione dioxime;

(1E)-1-phenyl-3-(4-pyrimidin-2-ylpiperazin-1-yl)propan-1-one oxime;

(1Z)-1-phenyl-3-(4-pyrimidin-2-ylpiperazin-1-yl)propan-1-one oxime;

1,5-diphenyl-2-[(4-pyrimidin-2-ylpiperazin-1-yl)methyl]pentane-1,5-dione

10 dioxime;

1-(4-fluorophenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one oxime;

(1E)-1-(4-chlorophenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one oxime;

(1E)-1-phenyl-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-ethyloxime;

15 (1Z)-1-phenyl-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-ethyloxime;

(1E)-1-phenyl-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-methyloxime;

(1Z)-1-phenyl-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-methyloxime;

(1E)-1-phenyl-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-propyloxime;

(1Z)-1-phenyl-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-propyloxime;

20 (1E)-1-phenyl-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-allyloxime;

(1Z)-1-phenyl-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-allyloxime;

(1E)-1-(3,5-difluorophenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-methyloxime;

(1Z)-1-(3,5-difluorophenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-

25 methyloxime;

({[1-phenyl-3-(4-pyridin-2-ylpiperazin-1-yl)propylidene]amino}oxy)acetonitrile;

1-phenyl-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-butyloxime;

(1E)-1-phenyl-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-

30 isopropyloxime;

(1E)-1-(3,5-dimethylphenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-methyloxime;

(1Z)-1-(3,5-dimethylphenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-methyloxime;

(1E)-1-(4-chloro-3-methylphenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-methyloxime;

(1Z)-1-(4-chloro-3-methylphenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-methyloxime;

5 (1E)-1-(2-naphthyl)-2-(4-pyridin-2-ylpiperazin-1-yl)ethanone O-methyloxime;

(1Z)-1-(2-naphthyl)-2-(4-pyridin-2-ylpiperazin-1-yl)ethanone O-methyloxime;

(1E)-1-(3-methylphenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-ethyloxime;

(1Z)-1-(3-methylphenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-ethyloxime;

10 1-(4-fluorophenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-(2,2,2-trifluoroethyl)oxime;

1-(4-chlorophenyl)-3-(methoxyamino)-2-[(4-pyridin-2-ylpiperazin-1-yl)methyl]propan-1-one O-methyloxime;

15 1-(4-chlorophenyl)-3-isopropoxy-2-[(4-pyridin-2-ylpiperazin-1-yl)methyl]propan-1-one O-methyloxime;

1-(4-chlorophenyl)-2-methyl-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-methyloxime;

(1E)-1-(3,4-dichlorophenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-methyloxime;

20 (1Z)-1-(3,4-dichlorophenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-methyloxime;

(1E)-1-(2-chlorophenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-methyloxime;

25 (1Z)-1-(2-chlorophenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-methyloxime;

(1E)-1-(2,4-dichlorophenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-methyloxime;

(1Z)-1-(2,4-dichlorophenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-methyloxime;

30 (1E)-1-(4-bromophenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-methyloxime;

(1Z)-1-(4-bromophenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-methyloxime;

(1E)-1-(3-fluorophenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-methyloxime;

(1Z)-1-(3-fluorophenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-methyloxime;

5 (1E)-1-(4-fluorophenyl)-2-(4-pyrimidin-2-ylpiperazin-1-yl)ethanone oxime;

(1Z)-1-(4-fluorophenyl)-2-(4-pyrimidin-2-ylpiperazin-1-yl)ethanone oxime;

(1E)-1-(4-fluorophenyl)-2-(4-pyridin-2-ylpiperazin-1-yl)ethanone oxime;

(1Z)-1-(4-fluorophenyl)-2-(4-pyridin-2-ylpiperazin-1-yl)ethanone oxime;

10 2-{4-[(3E)-3-(hydroxyimino)-3-phenylpropyl]piperazin-1-yl}nicotinonitrile;

2-{4-[(3Z)-3-(hydroxyimino)-3-phenylpropyl]piperazin-1-yl}nicotinonitrile;

1-phenyl-3-[4-(1,3-thiazol-2-yl)piperazin-1-yl]propan-1-one oxime;

1-phenyl-3-(4-pyrimidin-2-ylpiperazin-1-yl)propan-1-one O-ethyloxime;

1-phenyl-3-[4-(1,3-thiazol-2-yl)piperazin-1-yl]propan-1-one O-ethyloxime;

3-[4-(3-methylpyridin-2-yl)piperazin-1-yl]-1-phenylpropan-1-one O-

15 ethyloxime;

2-{4-[3-(ethoxyimino)-3-phenylpropyl]piperazin-1-yl}nicotinonitrile;

2-{4-[3-(ethoxyimino)-3-(3-methylphenyl)propyl]piperazin-1-yl}nicotinonitrile;

(1E)-1-(4-fluorophenyl)-2-[(2S)-2-methyl-4-pyridin-2-ylpiperazin-1-

20 yl]ethanone O-methyloxime;

(1Z)-1-(4-fluorophenyl)-2-[(2S)-2-methyl-4-pyridin-2-ylpiperazin-1-yl]ethanone O-methyloxime;

(1E)-1-(4-chlorophenyl)-3-[(2S)-2-methyl-4-pyridin-2-ylpiperazin-1-yl]propan-1-one O-methyloxime;

25 (1Z)-1-(4-chlorophenyl)-3-[(2S)-2-methyl-4-pyridin-2-ylpiperazin-1-yl]propan-1-one O-methyloxime;

1-(4-chlorophenyl)-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-(2-hydroxyethyl)oxime;

(1E)-1-(4-chlorophenyl)-3-[4-(5-hydroxypyridin-2-yl)piperazin-1-yl]propan-

30 1-one O-methyloxime;

(1Z)-1-(4-chlorophenyl)-3-[4-(5-hydroxypyridin-2-yl)piperazin-1-yl]propan-1-one O-methyloxime;

1-(4-fluorophenyl)-2-[4-(5-hydroxypyridin-2-yl)piperazin-1-yl]ethanone O-methyloxime;

(1E)-1-(4-chlorophenyl)-2-hydroxy-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-methyloxime;

(1Z)-1-(4-chlorophenyl)-2-hydroxy-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-methyloxime;

5 (1E)-1-(4-chlorophenyl)-3-(4-pyrimidin-2-ylpiperazin-1-yl)propan-1-one O-methyloxime;

(1Z)-1-(4-chlorophenyl)-3-(4-pyrimidin-2-ylpiperazin-1-yl)propan-1-one O-methyloxime;

10 (1E)-1-(4-chlorophenyl)-2-methoxy-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-methyloxime; and

(1Z)-1-(4-chlorophenyl)-2-methoxy-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-methyloxime.

6. The compound according to claim 2 wherein

15 X is O;

R<sub>2</sub> is arylalkyl;

Z is N;

--- is absent; and

R<sub>4</sub> is heteroaryl.

20

7. The compound according to claim 2 wherein

X is O;

R<sub>2</sub> is arylalkyl wherein the arylalkyl is benzyl;

Z is N;

25 --- is absent; and

R<sub>4</sub> is heteroaryl wherein the heteroaryl is selected from the group consisting of pyrazin-2-yl, 3-cyanopyridin-2-yl, 5-hydroxypyridin-2-yl, 3-methylpyridin-2-yl, pyridin-2-yl, 2-pyridinium N-oxide, pyrimidin-2-yl, and thiazol-2-yl.

30 8. The compound according to claim 7 selected from the group consisting of (2E)-1-phenyl-3-(4-pyridin-2-ylpiperazin-1-yl)acetone O-methyloxime; and (2Z)-1-phenyl-3-(4-pyridin-2-ylpiperazin-1-yl)acetone O-methyloxime.

9. The compound according to claim 2 wherein

- X is O;  
R<sub>2</sub> is heteroaryl;  
Z is N;  
--- is absent; and  
5 R<sub>4</sub> is heteroaryl.
10. The compound according to claim 2 wherein  
X is O;  
R<sub>2</sub> is heteroaryl wherein the heteroaryl is pyridin-3-yl;  
10 Z is N;  
--- is absent; and  
R<sub>4</sub> is heteroaryl wherein the heteroaryl is selected from the group consisting of  
pyrazin-2-yl, 3-cyanopyridin-2-yl, 5-hydroxypyridin-2-yl, 3-methylpyridin-2-yl,  
pyridin-2-yl, 2-pyridinium N-oxide, pyrimidin-2-yl, and thiazol-2-yl.  
15
11. The compound according to claim 4 selected from the group consisting of  
(1E)-1-pyridin-3-yl-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-  
methyloxime; and  
(1Z)-1-pyridin-3-yl-3-(4-pyridin-2-ylpiperazin-1-yl)propan-1-one O-  
20 methyloxime.
12. The compound according to claim 2 wherein  
X is O;  
R<sub>2</sub> is aryl;  
25 Z is C;  
--- is a single bond; and  
R<sub>4</sub> is heteroaryl.
13. The compound according to claim 2 wherein  
30 X is O;  
R<sub>2</sub> is aryl wherein the aryl is selected from the group consisting of naphthyl  
and phenyl wherein the phenyl is substituted with 0, 1, or 2 substituents independently  
selected from the group consisting of alkyl, cyano, and halogen;  
Z is C;



--- is a single bond; and

R<sub>4</sub> is heteroaryl wherein the heteroaryl is selected from the group consisting of pyrazin-2-yl, 3-cyanopyridin-2-yl, 5-hydroxypyridin-2-yl, 3-methylpyridin-2-yl, pyridin-2-yl, 2-pyridinium N-oxide, pyrimidin-2-yl, and thiazol-2-yl.

5

14. The compound according to claim 13 selected from the group consisting of 1-(4-fluorophenyl)-3-[4-(1,3-thiazol-2-yl)-3,6-dihydropyridin-1(2H)-yl]propan-1-one O-methyloxime;

10 (1E)-1-(4-chlorophenyl)-2-[4-(1,3-thiazol-2-yl)-3,6-dihydropyridin-1(2H)-yl]ethanone O-methyloxime;

(1Z)-1-(4-chlorophenyl)-2-[4-(1,3-thiazol-2-yl)-3,6-dihydropyridin-1(2H)-yl]ethanone O-methyloxime;

(1E)-1-(4-chlorophenyl)-3-(3-methyl-3',6'-dihydro-2,4'-bipyridin-1'(2'H)-yl)propan-1-one O-methyloxime; and

15 (1Z)-1-(4-chlorophenyl)-3-(3-methyl-3',6'-dihydro-2,4'-bipyridin-1'(2'H)-yl)propan-1-one O-methyloxime.

15. The compound according to claim 2 wherein

X is O;

20 R<sub>2</sub> is aryl;

Z is CH;

--- is absent; and

R<sub>4</sub> is heteroaryl.

25 16. The compound according to claim 2 wherein

X is O;

R<sub>2</sub> is aryl wherein the aryl is selected from the group consisting of naphthyl and phenyl wherein the phenyl is substituted with 0, 1, or 2 substituents independently selected from the group consisting of alkyl, cyano, and halogen;

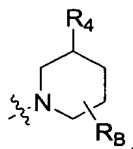
30 Z is CH;

--- is absent; and

R<sub>4</sub> is heteroaryl wherein the heteroaryl is selected from the group consisting of pyrazin-2-yl, 3-cyanopyridin-2-yl, 5-hydroxypyridin-2-yl, 3-methylpyridin-2-yl, pyridin-2-yl, 2-pyridinium N-oxide, pyrimidin-2-yl, and thiazol-2-yl.

17. The compound according to claim 16 selected from the group consisting of  
(1E)-1-(4-chlorophenyl)-3-(4-pyridin-2-ylpiperidin-1-yl)propan-1-one O-methyloxime;
- 5 (1Z)-1-(4-chlorophenyl)-3-(4-pyridin-2-ylpiperidin-1-yl)propan-1-one O-methyloxime;
- 2-{1-[(3E)-3-(4-chlorophenyl)-3-(methoxyimino)propyl]piperidin-4-yl}pyridinium N-oxide;
- 2-{1-[(3Z)-3-(4-chlorophenyl)-3-(methoxyimino)propyl]piperidin-4-yl}pyridinium N-oxide;
- 10 2-{1-[(2E)-2-(4-fluorophenyl)-2-(methoxyimino)ethyl]piperidin-4-yl}pyridinium N-oxide; and
- 2-{1-[(2Z)-2-(4-fluorophenyl)-2-(methoxyimino)ethyl]piperidin-4-yl}pyridinium N-oxide.
- 15
18. The compound according to claim 2 wherein  
X is NR<sub>A</sub>;  
R<sub>2</sub> is aryl;  
Z is N;
- 20 --- is absent; and  
R<sub>4</sub> is heteroaryl.
19. The compound according to claim 2 wherein  
X is NR<sub>A</sub>;
- 25 R<sub>2</sub> is aryl wherein the aryl is selected from the group consisting of naphthyl and phenyl wherein the phenyl is substituted with 0, 1, or 2 substituents independently selected from the group consisting of alkyl, cyano, and halogen;
- Z is N;
- is absent; and
- 30 R<sub>4</sub> is heteroaryl wherein the heteroaryl is selected from the group consisting of pyrazin-2-yl, 3-cyanopyridin-2-yl, 5-hydroxypyridin-2-yl, 3-methylpyridin-2-yl, pyridin-2-yl, 2-pyridinium N-oxide, pyrimidin-2-yl, and thiazol-2-yl.

20. The compound according to claim 19 that is 1-(4-fluorophenyl)-2-(4-pyridin-2-ylpiperazin-1-yl)ethanone methylhydrazone.
21. The compound according to claim 2 wherein  
 5 X is NR<sub>A</sub>;  
 R<sub>2</sub> is aryl;  
 Z is CH;  
 --- is absent; and  
 R<sub>4</sub> is heteroaryl.
- 10 22. The compound according to claim 2 wherein  
 X is NR<sub>A</sub>;  
 R<sub>2</sub> is aryl wherein the aryl is selected from the group consisting of naphthyl and phenyl wherein the phenyl is substituted with 0, 1, or 2 substituents independently  
 15 selected from the group consisting of alkyl, cyano, and halogen;  
 Z is CH;  
 --- is absent; and  
 R<sub>4</sub> is heteroaryl wherein the heteroaryl is selected from the group consisting of  
 20 pyrazin-2-yl, 3-cyanopyridin-2-yl, 5-hydroxypyridin-2-yl, 3-methylpyridin-2-yl,  
 pyridin-2-yl, 2-pyridinium N-oxide, pyrimidin-2-yl, and thiazol-2-yl.
23. The compound according to claim 22 that is 1-(4-fluorophenyl)-2-(4-pyridin-2-ylpiperidin-1-yl)ethanone methylhydrazone.
- 25 24. The compound according to claim 1 wherein R<sub>3</sub> is



25. The compound according to claim 24 wherein  
 R<sub>2</sub> is aryl; and  
 30 R<sub>4</sub> is heteroaryl.

26. The compound according to claim 24 wherein

R<sub>2</sub> is aryl wherein the aryl is selected from the group consisting of naphthyl and phenyl wherein the phenyl is substituted with 0, 1, or 2 substituents independently selected from the group consisting of alkyl, cyano, and halogen; and

5 R<sub>4</sub> is heteroaryl wherein the heteroaryl is selected from the group consisting of pyrazin-2-yl, 3-cyanopyridin-2-yl, 5-hydroxypyridin-2-yl, 3-methylpyridin-2-yl, pyridin-2-yl, 2-pyridinium N-oxide, pyrimidin-2-yl, and thiazol-2-yl.

27. The compound according to claim 26 selected from the group consisting of

10 1-(4-fluorophenyl)-3-[3-(1,3-thiazol-2-yl)piperidin-1-yl]propan-1-one O-methyloxime;

1-(4-fluorophenyl)-3-[3-(1,3-thiazol-2-yl)piperidin-1-yl]propan-1-one O-ethyloxime;

15 1-(4-fluorophenyl)-3-(3-pyridin-2-ylpiperidin-1-yl)propan-1-one O-methyloxime;

1-(4-chlorophenyl)-3-(3-pyridin-2-ylpiperidin-1-yl)propan-1-one O-methyloxime;

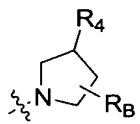
(1E)-1-(4-chlorophenyl)-3-[3-(1,3-thiazol-2-yl)piperidin-1-yl]propan-1-one O-methyloxime;

20 (1Z)-1-(4-chlorophenyl)-3-[3-(1,3-thiazol-2-yl)piperidin-1-yl]propan-1-one O-methyloxime;

2-{1-[2-(4-fluorophenyl)-2-(methoxyimino)ethyl]piperidin-3-yl}pyridinium N-oxide; and

25 2-{1-[3-(4-fluorophenyl)-3-(methoxyimino)propyl]piperidin-3-yl}pyridinium N-oxide.

28. The compound according to claim 1 wherein R<sub>3</sub> is



30 29. The compound according to claim 28 wherein

R<sub>2</sub> is aryl; and

R<sub>4</sub> is heteroaryl.

30. The compound according to claim 28 wherein  
R<sub>2</sub> is aryl wherein the aryl is selected from the group consisting of naphthyl  
and phenyl wherein the phenyl is substituted with 0, 1, or 2 substituents independently  
5 selected from the group consisting of alkyl, cyano, and halogen; and  
R<sub>4</sub> is heteroaryl wherein the heteroaryl is selected from the group consisting of  
pyrazin-2-yl, 3-cyanopyridin-2-yl, 5-hydroxypyridin-2-yl, 3-methylpyridin-2-yl,  
pyridin-2-yl, 2-pyridinium N-oxide, pyrimidin-2-yl, and thiazol-2-yl.
- 10 31. The compound according to claim 30 selected from the group consisting of  
(1E)-1-(4-fluorophenyl)-3-(3-pyrazin-2-ylpyrrolidin-1-yl)propan-1-one O-  
methyloxime;  
(1Z)-1-(4-fluorophenyl)-3-(3-pyrazin-2-ylpyrrolidin-1-yl)propan-1-one O-  
methyloxime;  
15 (1E)-1-(4-fluorophenyl)-2-(3-pyrazin-2-ylpyrrolidin-1-yl)ethanone O-  
methyloxime;  
(1Z)-1-(4-fluorophenyl)-2-(3-pyrazin-2-ylpyrrolidin-1-yl)ethanone O-  
methyloxime;  
(1E)-1-(4-fluorophenyl)-3-(3-pyrazin-2-ylpyrrolidin-1-yl)propan-1-one oxime;  
20 (1Z)-1-(4-fluorophenyl)-3-(3-pyrazin-2-ylpyrrolidin-1-yl)propan-1-one oxime;  
and  
(1Z)-1-(4-fluorophenyl)-2-(3-pyrazin-2-ylpyrrolidin-1-yl)ethanone oxime.
32. A pharmaceutical composition comprising a therapeutically effective amount  
25 of a compound of formula (I) in combination with a pharmaceutically acceptable  
carrier.
33. A method of treating sexual dysfunction in a mammal comprising  
administering to the mammal a therapeutically effective amount of a compound of  
30 formula (I) or a pharmaceutically acceptable salt or prodrug thereof in combination  
with a pharmaceutically acceptable carrier.
34. A method of treating sexual dysfunction in a mammal comprising  
administering to the mammal a therapeutically effective amount of a compound of

formula (I) or a pharmaceutically acceptable salt or prodrug thereof in combination with a phosphodiesterase 5 inhibitor.

35. A method of treating sexual dysfunction in a mammal comprising  
5 administering to the mammal a therapeutically effective amount of a compound of formula (I) or a pharmaceutically acceptable salt or prodrug thereof in combination with an adrenergic receptor antagonist.
36. A method of treating sexual dysfunction in a mammal comprising  
10 administering to the mammal a therapeutically effective amount of a compound of formula (I) or a pharmaceutically acceptable salt or prodrug thereof in combination with a dopamine agonist.
37. A method of treating male erectile dysfunction in a mammal comprising  
15 administering to the mammal in need of such treatment a therapeutically effective amount of a compound of formula (I) or a pharmaceutically acceptable salt or prodrug thereof.
38. A method of treating female sexual dysfunction in a mammal comprising  
20 administering to the mammal in need of such treatment a therapeutically effective amount of a compound of formula (I) or a pharmaceutically acceptable salt or prodrug thereof.
39. A method of treating cardiovascular disorders, inflammatory disorders,  
25 attention deficit hyperactivity disorder, Alzheimer's disease, drug abuse, Parkinson's disease, schizophrenia, anxiety, mood disorders or depression in a mammal comprising administering to the mammal in need of such treatment a therapeutically effective amount of a compound of formula (I) or a pharmaceutically acceptable salt or prodrug thereof.  
30
40. A method of treating sexual dysfunction in a mammal comprising  
administering to the mammal a therapeutically effective amount of a compound of formula (Ia)



R<sub>2</sub> is aryl;  
Z is N;  
--- is absent; and  
R<sub>4</sub> is heteroaryl.

5

43. The method according to claim 41 wherein  
X is O;  
R<sub>2</sub> is aryl wherein the aryl is selected from the group consisting of naphthyl  
and phenyl wherein the phenyl is substituted with 0, 1, or 2 substituents independently  
10 selected from the group consisting of alkyl, cyano, and halogen;  
Z is N;  
--- is absent; and  
R<sub>4</sub> is heteroaryl wherein the heteroaryl is selected from the group consisting of  
pyrazin-2-yl, 3-cyanopyridin-2-yl, 5-hydroxypyridin-2-yl, 3-methylpyridin-2-yl,  
15 pyridin-2-yl, 2-pyridinium N-oxide, pyrimidin-2-yl, and thiazol-2-yl.

44. The method according to claim 43 where the compound of formula Ia is  
selected from the group consisting of  
(1E)-1-(4-fluorophenyl)-4-(4-pyridin-2ylpiperazin-1-yl)butan-1-one oxime;  
20 (1Z)-1-(4-fluorophenyl)-4-(4-pyridin-2ylpiperazin-1-yl)butan-1-one oxime;  
(1E)-1-(4-fluorophenyl)-4-(4-pyridin-2ylpiperazin-1-yl)butan-1-one  
methyloxime; and  
(1E)-1-(4-fluorophenyl)-4-(4-pyridin-2ylpiperazin-1-yl)butan-1-one  
methyloxime.

25

45. The method according to claim 41 wherein  
X is O;  
R<sub>2</sub> is arylalkyl;  
Z is N;  
30 --- is absent; and  
R<sub>4</sub> is heteroaryl.

46. The method according to claim 41 wherein  
X is O;



R<sub>2</sub> is arylalkyl wherein the arylalkyl is benzyl;

Z is N;

--- is absent; and

5 R<sub>4</sub> is heteroaryl wherein the heteroaryl is selected from the group consisting of  
pyrazin-2-yl, 3-cyanopyridin-2-yl, 5-hydroxypyridin-2-yl, 3-methylpyridin-2-yl,  
pyridin-2-yl, 2-pyridinium N-oxide, pyrimidin-2-yl, and thiazol-2-yl.

47. The method according to claim 41 wherein

X is O;

10 R<sub>2</sub> is heteroaryl;

Z is N;

--- is absent; and

R<sub>4</sub> is heteroaryl.

15 48. The method according to claim 41 wherein

X is O;

R<sub>2</sub> is heteroaryl wherein the heteroaryl is pyridin-3-yl;

Z is N;

--- is absent; and

20 R<sub>4</sub> is heteroaryl wherein the heteroaryl is selected from the group consisting of  
pyrazin-2-yl, 3-cyanopyridin-2-yl, 5-hydroxypyridin-2-yl, 3-methylpyridin-2-yl,  
pyridin-2-yl, 2-pyridinium N-oxide, pyrimidin-2-yl, and thiazol-2-yl.

49. The method according to claim 41 wherein

25 X is O;

R<sub>2</sub> is aryl;

Z is C;

--- is a single bond; and

R<sub>4</sub> is heteroaryl.

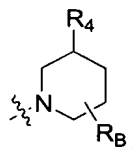
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50. The method according to claim 41 wherein

X is O;

- R<sub>2</sub> is aryl wherein the aryl is selected from the group consisting of naphthyl and phenyl wherein the phenyl is substituted with 0, 1, or 2 substituents independently selected from the group consisting of alkyl, cyano, and halogen;
- Z is C;
- 5 --- is a single bond; and
- R<sub>4</sub> is heteroaryl wherein the heteroaryl is selected from the group consisting of pyrazin-2-yl, 3-cyanopyridin-2-yl, 5-hydroxypyridin-2-yl, 3-methylpyridin-2-yl, pyridin-2-yl, 2-pyridinium N-oxide, pyrimidin-2-yl, and thiazol-2-yl.
- 10 51. The method according to claim 41 wherein
- X is O;
- R<sub>2</sub> is aryl;
- Z is CH;
- is absent; and
- 15 R<sub>4</sub> is heteroaryl.
52. The method according to claim 41 wherein
- X is O;
- R<sub>2</sub> is aryl wherein the aryl is selected from the group consisting of naphthyl
- 20 and phenyl wherein the phenyl is substituted with 0, 1, or 2 substituents independently selected from the group consisting of alkyl, cyano, and halogen;
- Z is CH;
- is absent; and
- R<sub>4</sub> is heteroaryl wherein the heteroaryl is selected from the group consisting of
- 25 pyrazin-2-yl, 3-cyanopyridin-2-yl, 5-hydroxypyridin-2-yl, 3-methylpyridin-2-yl, pyridin-2-yl, 2-pyridinium N-oxide, pyrimidin-2-yl, and thiazol-2-yl.
53. The method according to claim 41 wherein
- X is NR<sub>A</sub>;
- 30 R<sub>2</sub> is aryl;
- Z is N;
- is absent; and
- R<sub>4</sub> is heteroaryl.

54. The method according to claim 41 wherein  
X is NR<sub>A</sub>;  
R<sub>2</sub> is aryl wherein the aryl is selected from the group consisting of naphthyl  
and phenyl wherein the phenyl is substituted with 0, 1, or 2 substituents independently  
5 selected from the group consisting of alkyl, cyano, and halogen;  
Z is N;  
--- is absent; and  
R<sub>4</sub> is heteroaryl wherein the heteroaryl is selected from the group consisting of  
pyrazin-2-yl, 3-cyanopyridin-2-yl, 5-hydroxypyridin-2-yl, 3-methylpyridin-2-yl,  
10 pyridin-2-yl, 2-pyridinium N-oxide, pyrimidin-2-yl, and thiazol-2-yl.
55. The method according to claim 41 wherein  
X is NR<sub>A</sub>;  
R<sub>2</sub> is aryl;  
15 Z is CH;  
--- is absent; and  
R<sub>4</sub> is heteroaryl.
56. The method according to claim 41 wherein  
20 X is NR<sub>A</sub>;  
R<sub>2</sub> is aryl wherein the aryl is selected from the group consisting of naphthyl  
and phenyl wherein the phenyl is substituted with 0, 1, or 2 substituents independently  
selected from the group consisting of alkyl, cyano, and halogen;  
Z is CH;  
25 --- is absent; and  
R<sub>4</sub> is heteroaryl wherein the heteroaryl is selected from the group consisting of  
pyrazin-2-yl, 3-cyanopyridin-2-yl, 5-hydroxypyridin-2-yl, 3-methylpyridin-2-yl,  
pyridin-2-yl, 2-pyridinium N-oxide, pyrimidin-2-yl, and thiazol-2-yl.
- 30 57. The method according to claim 41 wherein R<sub>3</sub> is



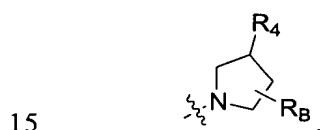
58. The method according to claim 57 wherein  
R<sub>2</sub> is aryl; and  
R<sub>4</sub> is heteroaryl.

5

59. The method according to claim 57 wherein  
R<sub>2</sub> is aryl wherein the aryl is selected from the group consisting of naphthyl  
and phenyl wherein the phenyl is substituted with 0, 1, or 2 substituents independently  
selected from the group consisting of alkyl, cyano, and halogen; and

10 R<sub>4</sub> is heteroaryl wherein the heteroaryl is selected from the group consisting of  
pyrazin-2-yl, 3-cyanopyridin-2-yl, 5-hydroxypyridin-2-yl, 3-methylpyridin-2-yl,  
pyridin-2-yl, 2-pyridinium N-oxide, pyrimidin-2-yl, and thiazol-2-yl.

60. The method according to claim 40 wherein R<sub>3</sub> is



61. The method according to claim 60 wherein  
R<sub>2</sub> is aryl; and  
R<sub>4</sub> is heteroaryl.

20

62. The method according to claim 60 wherein  
R<sub>2</sub> is aryl wherein the aryl is selected from the group consisting of naphthyl  
and phenyl wherein the phenyl is substituted with 0, 1, or 2 substituents independently  
selected from the group consisting of alkyl, cyano, and halogen; and

25 R<sub>4</sub> is heteroaryl wherein the heteroaryl is selected from the group consisting of  
pyrazin-2-yl, 3-cyanopyridin-2-yl, 5-hydroxypyridin-2-yl, 3-methylpyridin-2-yl,  
pyridin-2-yl, 2-pyridinium N-oxide, pyrimidin-2-yl, and thiazol-2-yl.

63. A pharmaceutical composition comprising a therapeutically effective amount  
30 of a compound of formula (Ia) in combination with a pharmaceutically acceptable  
carrier.

64. A method of treating sexual dysfunction in a mammal comprising administering to the mammal a therapeutically effective amount of a compound of formula (I) or a pharmaceutically acceptable salt or prodrug thereof in combination with a pharmaceutically acceptable carrier.

5

65. A method of treating sexual dysfunction in a mammal comprising administering to the mammal a therapeutically effective amount of a compound of formula (Ia) or a pharmaceutically acceptable salt or prodrug thereof in combination with a phosphodiesterase 5 inhibitor.

10

66. A method of treating sexual dysfunction in a mammal comprising administering to the mammal a therapeutically effective amount of a compound of formula (Ia) or a pharmaceutically acceptable salt or prodrug thereof in combination with an adrenergic receptor antagonist.

15

67. A method of treating sexual dysfunction in a mammal comprising administering to the mammal a therapeutically effective amount of a compound of formula (Ia) or a pharmaceutically acceptable salt or prodrug thereof in combination with a dopamine agonist.

20

68. A method of treating male erectile dysfunction in a mammal comprising administering to the mammal in need of such treatment a therapeutically effective amount of a compound of formula (Ia) or a pharmaceutically acceptable salt or prodrug thereof.

25

69. A method of treating female sexual dysfunction in a mammal comprising administering to the mammal in need of such treatment a therapeutically effective amount of a compound of formula (Ia) or a pharmaceutically acceptable salt or prodrug thereof.

30

70. A method of treating cardiovascular disorders, attention deficit hyperactivity disorder, Alzheimer's disease, drug abuse, Parkinson's disease, schizophrenia, anxiety, mood disorders or depression in a mammal comprising administering to the mammal

in need of such treatment a therapeutically effective amount of a compound of formula (Ia) or a pharmaceutically acceptable salt or prodrug thereof.

71. A compound of formula (II)



or a pharmaceutically acceptable salt or prodrug thereof, wherein

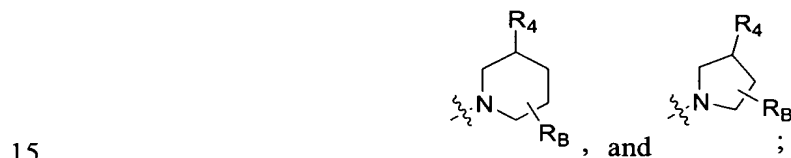
X is selected from the group consisting of O and NR<sub>A</sub>;

R<sub>A</sub> is selected from the group consisting of hydrogen and alkyl;

10 R<sub>1</sub> is selected from the group consisting of hydrogen, alkenyl, alkoxyalkyl, alkyl, alkynyl, arylalkyl, cyanoalkyl, cycloalkyl, haloalkyl, and hydroxyalkyl;

R<sub>2</sub> is selected from the group consisting of aryl, arylalkyl, heteroaryl, and heteroarylalkyl;

R<sub>3</sub> is selected from the group consisting of



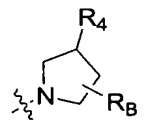
R<sub>4</sub> is aryl;

L is alkylene substituted with 0 or 1 substituent selected from the group consisting of alkoxy, alkoxyamino, hydroxy, and hydroxyiminoaryl; and

R<sub>B</sub> is selected from the group consisting of hydrogen and alkyl.

20

72. The compound according to claim 70 wherein R<sub>3</sub> is



73. The compound according to claim 72 wherein

25 R<sub>2</sub> is aryl; and

R<sub>4</sub> is aryl.

74. The compound according to claim 72 wherein

R<sub>2</sub> is aryl wherein the aryl is selected from the group consisting of naphthyl and phenyl wherein the phenyl is substituted with 0, 1, or 2 substituents independently selected from the group consisting of alkyl, cyano, and halogen; and

5 R<sub>4</sub> is aryl wherein the aryl is phenyl substituted with 0 or 1 substituent selected from the group consisting of alkoxy, cyano, and haloalkyl.

75. The compound according to claim 74 selected from the group consisting of

(1E)-1-(4-fluorophenyl)-3-{3-[3-(trifluoromethyl)phenyl]pyrrolidin-1-yl}propan-1-one O-methyloxime;

(1Z)-1-(4-fluorophenyl)-3-{3-[3-(trifluoromethyl)phenyl]pyrrolidin-1-yl}propan-1-one O-methyloxime;

1-(4-fluorophenyl)-3-[3-(2-methoxyphenyl)pyrrolidin-1-yl]propan-1-one O-methyloxime;

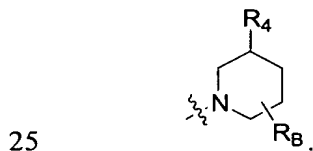
15 (1E)-1-(4-fluorophenyl)-3-[3-(3-methoxyphenyl)pyrrolidin-1-yl]propan-1-one O-methyloxime;

(1Z)-1-(4-fluorophenyl)-3-[3-(3-methoxyphenyl)pyrrolidin-1-yl]propan-1-one O-methyloxime;

(1E)-1-(4-fluorophenyl)-3-[3-(4-methoxyphenyl)pyrrolidin-1-yl]propan-1-one O-methyloxime; and

20 (1Z)-1-(4-fluorophenyl)-3-[3-(4-methoxyphenyl)pyrrolidin-1-yl]propan-1-one O-methyloxime.

76. The compound according to claim 70 wherein R<sub>3</sub> is



77. The compound according to claim 76 wherein

R<sub>2</sub> is aryl; and

R<sub>4</sub> is aryl.

30

78. The compound according to claim 76 wherein

R<sub>2</sub> is aryl wherein the aryl is selected from the group consisting of naphthyl and phenyl wherein the phenyl is substituted with 0, 1, or 2 substituents independently selected from the group consisting of alkyl, cyano, and halogen; and

R<sub>4</sub> is aryl wherein the aryl is phenyl substituted with 0 or 1 substituent selected from the group consisting of alkoxy, cyano, and haloalkyl.

79. The compound according to claim 78 selected from the group consisting of 1-(4-fluorophenyl)-3-(3-phenylpiperidin-1-yl)propan-1-one O-methyloxime; 1-phenyl-3-(3-phenylpiperidin-1-yl)propan-1-one O-methyloxime; and 1-(4-chlorophenyl)-3-(3-phenylpiperidin-1-yl)propan-1-one O-methyloxime.

80. A pharmaceutical composition comprising a therapeutically effective amount of a compound of formula (II) in combination with a pharmaceutically acceptable carrier.

81. A method of treating sexual dysfunction in a mammal comprising administering to the mammal a therapeutically effective amount of a compound of formula (II) or a pharmaceutically acceptable salt or prodrug thereof in combination with a pharmaceutically acceptable carrier.

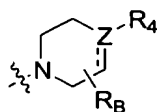
82. A method of treating sexual dysfunction in a mammal comprising administering to the mammal a therapeutically effective amount of a compound of formula (II) or a pharmaceutically acceptable salt or prodrug thereof in combination with a phosphodiesterase 5 inhibitor.

83. A method of treating sexual dysfunction in a mammal comprising administering to the mammal a therapeutically effective amount of a compound of formula (II) or a pharmaceutically acceptable salt or prodrug thereof in combination with an adrenergic receptor antagonist.

84. A method of treating sexual dysfunction in a mammal comprising administering to the mammal a therapeutically effective amount of a compound of formula (II) or a pharmaceutically acceptable salt or prodrug thereof in combination with a dopamine agonist.







R<sub>4</sub> is aryl;

L is alkylene substituted with 0 or 1 substituent selected from the group consisting of alkoxy, alkoxyamino, hydroxy, and hydroxyiminoaryl;

5 R<sub>B</sub> is selected from the group consisting of hydrogen and alkyl;

Z is selected from the group consisting of C and CH; and

--- is absent or a single bond provided that when Z is C then --- is a single bond.

10 89. A pharmaceutical composition comprising a therapeutically effective amount of a compound of formula (III) in combination with a pharmaceutically acceptable carrier.

15 90. A method of treating sexual dysfunction in a mammal comprising administering to the mammal a therapeutically effective amount of a compound of formula (III) or a pharmaceutically acceptable salt or prodrug thereof in combination with a pharmaceutically acceptable carrier.

20 91. A method of treating sexual dysfunction in a mammal comprising administering to the mammal a therapeutically effective amount of a compound of formula (III) or a pharmaceutically acceptable salt or prodrug thereof in combination with a phosphodiesterase 5 inhibitor.

25 92. A method of treating sexual dysfunction in a mammal comprising administering to the mammal a therapeutically effective amount of a compound of formula (III) or a pharmaceutically acceptable salt or prodrug thereof in combination with an adrenergic receptor antagonist.

30 93. A method of treating sexual dysfunction in a mammal comprising administering to the mammal a therapeutically effective amount of a compound of formula (III) or a pharmaceutically acceptable salt or prodrug thereof in combination with a dopamine agonist.

94. A method of treating male erectile dysfunction in a mammal comprising administering to the mammal in need of such treatment a therapeutically effective amount of a compound of formula (III) or a pharmaceutically acceptable salt or  
5 prodrug thereof.

95. A method of treating female sexual dysfunction in a mammal comprising administering to the mammal in need of such treatment a therapeutically effective amount of a compound of formula (III) or a pharmaceutically acceptable salt or  
10 prodrug thereof.

96. A method of treating cardiovascular disorders, inflammatory disorders, attention deficit hyperactivity disorder, Alzheimer's disease, drug abuse, Parkinson's disease, schizophrenia, anxiety, mood disorders or depression in a mammal  
15 comprising administering to the mammal in need of such treatment a therapeutically effective amount of a compound of formula (III) or a pharmaceutically acceptable salt or prodrug thereof.